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MEGAVOLT ELECTRON IRRADIATION FOR LOCALIZED MYCOSIS FUNGOIDES

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It is now known that mycosis fungoides is characteristically a T-cell lymphoma of undetermined cause arising from the skin (EDELSON 1980). The natural course of the disease is usually indolent originating from one area of the cutaneous system but later spreading to involve the entire body surface and eventually becoming a systemic disorder leading to a fatal outcome. The duration from onset and diagnosis of the disease to dissemination varies greatly and is usually totally unpredictable. However, once skin lesions become generalized, the chance of cure is very small (EPSTEIN et coll. 1972). A retrospective analysis was carried out to evaluate the effectiveness of small field megavolt electron irradiation for localized cutaneous mycosis fungoides and to determine whether curative treatment for this disease was possible if the diagnosis was made early while extent of skin involvement was still limited.

Materials and Methods

Records of all patients with cutaneous lymphoma treated in this Department at the Massachusetts Institute of Technology High Voltage Research Laboratory between 1964 and 1973 were reviewed. All these patients were treated with a constant potential electrostatic generator of the Van de Graaff type with the capacity of producing electrons with energies up to 3.5 MeV. The physical aspects and depth dose characteristics of the generator have been described previously (TRUMP et coll. 1953). The policy under review had been to employ local field electron beam with generous margins for limited disease and total skin electron irradiation for multiple lesions or diffuse disease covering at least 50 per

cent of the entire body surface. The technique of total skin electron irradiation has also been described previously (FROMER et coll. 1961, SMEDAL et coll. 1962, LO et coll. 1979b). Whenever small field irradiation was delivered, masonites or wood was used to shield uninvolved areas of the body surface.

During the period between 1964 and 1973, 14 new patients with localized cutaneous disease and 200 new patients with generalized cutaneous disease were treated. Localized disease is defined as skin involvement covering less than 25 per cent of total body surface. All patients who had clinical evidence of nodal or systemic involvement at the initial presentation were excluded. All the patients had skin biopsy indicating mycosis fungoides or lymphoma cutis, and all were followed up for a minimum of 5 years. None with generalized exfoliative erythroderma had more than 10 per cent circulating Sézary cells. The distribution of the patients by types of lesions appears in Table 1. It is conceivable that many patients with early lesions were not referred for electron irradiation as they were treated by dermatologists with topical agents for unbiopsied 'benign' lesions or even proven malignant disease.

Results

Of the 14 patients with localized cutaneous disease, 7 were men and 7 were women. All were irradiated with local fields with generous margins. Ten are at present living with no evidence of disease (NED; Table 2). The types of lesions and duration of survival of these 10 patients appear in Table 3. Although 3 of the 10 patients required more than

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one course of electron irradiation, the last course was administered at least 5 years ago. The overall 5-year disease-free survival rate was 71 per cent.

Of the 4 remaining patients, one died from surgical complications after a later abdominal exploration and detection of widespread visceral metastasis with local skin lesions controlled. Two patients are living with disease at present, and one recently died from disseminated involvement.

The sites of disease and doses given to the 10 patients with localized mycosis fungoides who are considered cured are given in Table 4. None of these patients received a total dose higher than 20 Gy. This confirms the extreme sensitivity of this disease to radiation. High total dose was not necessary, and further irradiation could be given safely when indicated without sacrificing a good chance for cure.

Many patients with recurrent disease after repeated courses of photon irradiation were still eligible for electron irradiation, if no chronic skin change from previous irradiation was present, because of the unique depth dose characteristics of megavolt electrons. A reasonable dose could still be delivered safely with good response (Table 4).

In contrast, of the 200 patients with generalized cutaneous disease treated with total skin electron irradiation, only 16 patients survived free of disease at 5 years, representing a cure rate of 8 per cent (LO et coll. 1979a; Table 5). Two of these 16 patients received more than one course of electron irradiation.

As a comparison, during the same period of time, 42 patients with skin involvement from systemic lymphoma were treated, and 40 of them received total skin electron irradiation. The median survival of this group of patients was 7 months. Only 2 patients are alive, and only one of them is clinically free of disease after combined irradiation and chemotherapy.

Discussion

Megavolt electron irradiation was first introduced in 1951 for treatment of cutaneous lymphoma (TRUMP et coll.) and remains one of the most effective means of therapy for this disease today (LEVI & WIERNIK 1975, EDELSON). Other modalities, including 8-methoxypsoralen (psoralen) followed by high-intensity longwave ultraviolet light (PUVA; GILCHREST et coll. 1976) and topical agents, such as steroids, nitrogen mustard (VONDERHEID et coll.

Table 1

Distribution of patients by types of lesions

Lesion	Localized	Generalized
Erythroderma	1	57
Plaque	4	89
Tumor	9	54
Total	14	200

Table 2

Localized cutaneous disease. Five-year survival with no evidence of disease

Lesion	No. of cases	Survivors
Erythroderma	1	1
Plaque	4	3*
Tumor	9	6**
Total	14	10

* One patient was given repeated treatments.

** Two patients were given repeated treatments.

Table 3

Localized cutaneous disease. Survival with no evidence of disease

Case No.	Lesion	Survival (years)	
		Since first treatment	Since last treatment
1	Erythroderma	8	8
2	Plaque	10	10
3	Plaque	8	8
4*	Plaque	8	5
5	Tumor	12	12
6*	Tumor	11	9
7	Tumor	10	10
8	Tumor	10	10
9	Tumor	6	6
10*	Tumor	6	5

* Patients given more than one course of electron treatment.

1979), and nitrosourea (ZACKHEIM et coll. 1979), are also of value in treating patients with mycosis fungoides with only skin involvement. Unfortunately, it has been shown that once this disease has become generalized, involving greater than 50 per cent of the entire body surface, any of these therapeutic

Table 4*Electron treatment for localized cutaneous disease*

Case No.	Lesion	Previous photon irradiation	Site(s)	Total dose* (Gy)/No. of fractions
1	Erythroderma	—	Upper extremities	3/1
2	Plaque	—	Upper extremities, back, left knee	6/3
3	Plaque	—	Lower extremities, left shoulder, lower abdomen	6/3
4**	Plaque	—	Face	10/5
5	Tumor	+	Back	18/8
6**	Tumor	+	Right thigh	8/4
7	Tumor	+	Right buttock	11/5
8	Tumor	—	Back	12/6
9	Tumor	—	Upper extremities, back	20/7
10**	Tumor	—	Right eyelids	10/2

* Total dose during the initial course of electron treatment.

** Patients given more than one course of electron treatment.

Table 5*Generalized cutaneous disease. Five-year survival with no evidence of disease*

Lesion	No. of cases	Survivors
Erythroderma	57	11
Plaque	89	2
Tumor	54	3*
Total	200	16

* Two patients were given repeated treatments.

modalities, regardless of whether there was a response, failed to affect survival (EPSTEIN et coll.). Even with total skin electron irradiation, our experience and that of others showed that the chance of cure was extremely remote (MEYLER et coll. 1978, BLASKO et coll. 1979, LO et coll. 1979 a, WALLNER et coll. 1979), particularly in the group of patients with tumor lesions (HOPPE et coll. 1977, LO et coll. 1979 b). Trials of adjuvant topical and systemic chemotherapy are now in progress with pending results (PRICE et coll. 1977, GRIEM et coll. 1979, WALLNER et coll.).

The present data confirmed that, in patients without extracutaneous disease, the most significant factor that determined duration of disease-free survival

was the extent of skin involvement at the initial presentation. Ten of the 14 patients (71 per cent) survived free of disease at least 5 years after the last course of local megavolt electron irradiation and can be considered cured. Seven of these patients received only one single course of electron beam therapy. Others have shown that chemotherapy might be equally effective in controlling limited disease (VONDERHEID et coll.). In contrast, LO et coll. (1979 a) in a previous report showed that only 16 of 200 patients with generalized cutaneous disease were cured after total skin electron irradiation. A parallel finding has been reported by the Stanford group (HOPPE et coll.). With total skin electron irradiation, the probability of complete continuous remission 5 years after therapy in their group of patients with limited plaque disease was 43 per cent as compared with 17 per cent in the group with generalized plaque disease.

As in the Stanford series, a high dose was not necessary for control of limited cutaneous mycosis fungoides. Of the 10 patients with localized disease considered cured, none received a total dose higher than 20 Gy. All of the Stanford patients with limited plaque lesions attained complete remission with a similar dose as low as 20 Gy (HOPPE et coll.). The implication is that repeated courses of electron beam therapy are feasible when indicated without sacrificing a good chance for cure.

The most exciting finding in the present review was that among the 10 patients with limited disease successfully treated with local field megavolt electron irradiation, the majority of them had tumorous lesions (Table 3). This indicates a remarkable prognostic dissimilarity between treated patients with localized tumorous disease and those with generalized tumorous lesions.

From the results of the present review the potential for cure is definitely demonstrated with megavolt electron beam therapy in patients with early localized mycosis fungoides.

SUMMARY

A retrospective analysis was carried out to evaluate the effectiveness of small field megavolt electron irradiation for localized mycosis fungoides. Only local field electron beam therapy was employed for limited disease reserving total skin electron irradiation for multiple lesions or diffuse disease covering at least 25 per cent of the entire body surface. Of the 14 patients with limited disease treated between 1964 and 1973 with the local field technique, 10 patients (71 per cent) are alive without evidence of disease at a minimum of 5 years. In contrast, of 200 patients with extensive cutaneous disease who received total skin electron irradiation, only 16 (8 per cent) were considered cured. It is concluded that early localized mycosis fungoides is potentially curable, and that limited field electron beam therapy with a relatively low total dose is adequate to obtain excellent response.

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